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EXAMINER
SIEW, J

ART UNIT	PAPER NUMBER
1653	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/020,743

Applicant(s)

Mack

Examiner

Jeffrey Siew

Group Art Unit

1653



☒ Responsive to communication(s) filed on Aug 16, 1999

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-10, 12-34, and 36-48 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-10, 12-34, and 36-48 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 10 & 13

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED ACTION

1. The response filed on August 16, 1999 has been fully considered and deemed persuasive in part. The amendments to overcome the 112 second paragraph rejections have been deemed persuasive. Concerning claims 19 & 43, the response argues that Zhao et al does not teach a third axis and that 3D graphs are difficult to comprehend. The use of 3D graphs in data analysis was well known and commonly practiced in the biological arts. Zhao et al has already shown data analysis of gene expression using two axes. One of ordinary skill in the art at the time of the invention would have been motivated to apply the use of a third axis and to extend Zhao et al's data analysis technique in order to further compare more samples simultaneously. The rejection is maintained.

THE FOLLOWING IS A NEW GROUND OF REJECTION NECESSITATED BY THE
AMENDMENT

Claim Rejections - 35 USC § 103

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2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) a patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. Claims 1-5, 20,21 & 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhao et al (Gene Vol. 156 pp. 207-213 1995) in view of Seilhamer et al (WO96/23078 1 August 1996).

Claims 1-5, 20,21 & 23 are drawn to displaying expression levels or compound concentration of two samples on a graph in which the first axis corresponds to expression level of first sample and the second axis is perpendicular to first axis and corresponds to expression level of second sample. A mark is displayed and in response to user's input, information about said selected expressed sequence is displayed.

Zhao et al teach bioimaging analyzer system to compare the expression profiles of thousands of genes cDNAs) simultaneously . They teach the a high density cDNA filter analysis in which expression profiles of 2505 cloned human brain cDNAs (genes) were monitored (see whole document esp. Abstract). Zhao et al teach that the cDNA probes were sequenced and compared with those in GenBank DNA nucleotide sequence Database by BLASTN program prior to preparing the filter. A quantitative analysis of the filter is performed using Fuji Bioimaging Analyzer BAS2000 System and automated quantification program AutoQuant. The final part is

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sequence analysis in which each clone is characterized by homology search in the GENBANK nucleotide Sequence Database (see page 208 & Figure 1). They applied the system for the comparative analysis of expression profile of the human cDNAs in brain. The expression profiles were illustrated on graphs by comparing the their scores from two tissues with Microsoft Excel (Microsoft) on a Macintosh personal computer(see page 210-211 and fig. 3). A mark for each gene is positioned relative to the expression levels in the two different samples. Although the reference is silent to the teaching of processor, memory and display, the personal computer inherently contains a display, microprocessor and memory in the form of RAM, ROM and hard disk.

Zhao et al do not teach an input from user and returning information of the selected expressed sequence.

Seilhamer et al teach preparing a relational database for a computer system that contains cDNA sequencing data and corresponding match logs indicating a correlation between presently identified cDNA sequences and previously known sequences. These databases may be organized in a table. They teach that a researcher to search the relational database using keywords or a query and to specify a search on the table to seek out specific information (See all of page 17). They teach that these databases and queries assist the scientist in performing many and various data analysis tasks.

One of ordinary skill in the art would have been motivated to apply Seilhamer et al's use of database in a computer system to Zhao et al's computer system and method of analyzing

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expression in samples in order to quickly allow user to gain information on the expressed sequences. Zhao et al states that the sequences for the cDNA probes were determined prior to preparing the filter. It would have been prima facie obvious to one of ordinary skill in the art to incorporate Zhao predetermined sequence information into a Seilhamer et al's database for the computer in order to allow the practitioner to input a query and easily access to information to assist in various data analysis tasks.

4. Claims 25-29,36-42,44,45,47 & 48 are rejected under 35 U.S.C. 103(a) as obvious over Zhao et al (Gene Vol. 156 pp. 207-213 1995) in view of Seilhamer et al (WO96/23078 1 August 1996).

Claims 25-29,36-42,44 & 45 are drawn to a software product that contains code that displays on first axis expression level or compound in first sample, displays on second axis an expression level or compound in second sample, displays a mark whose position is relative to first or second axis. Moreover, the code receives a response to user's input, information about said selected expressed sequence is displayed.

Claim 47 is drawn to computer system comprising display, processor and memory for displaying a first axis corresponding to expression level of first axis, code for displaying a first axis corresponding to expression level of first axis, code for displaying a mark, code for receiving a

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response to user's input and displaying information about said selected expressed sequence and a computer readable storage medium for storing codes.

Claims 48 is drawn to computer system comprising display, processor and memory for displaying a first axis corresponding to a compound concentration, code for displaying a first axis corresponding to compound concentration, code for displaying a mark, code for receiving a response to user's input and displaying information about said selected expressed sequence and a computer readable storage medium for storing codes.

Zhao et al teach bioimaging analyzer system to compare the expression profiles of thousands of genes cDNAs simultaneously. They teach a high density cDNA filter analysis in which expression profiles of 2505 cloned human brain cDNAs (genes) were monitored (see whole document esp. Abstract). Zhao et al also teaches that the cDNA probes were sequenced and compared with those in GenBank DNA nucleotide sequence Database by BLASTN program prior to preparing the filter. A quantitative analysis of the filter is performed using Fuji Bioimaging Analyzer BAS2000 System and automated quantification program AutoQuant. The final part is sequence analysis in which each clone is characterized by homology search in the GENBANK nucleotide Sequence Database (see page 208 & Figure 1). They applied the system for the comparative analysis of expression profile of the human cDNAs in brain. The expression profiles were illustrated on graphs by comparing the their scores from two tissues with Microsoft Excel (Microsoft) on a Macintosh personal computer(see page 210-211 and fig. 3). A mark for each gene is positioned relative to the expression levels in the two different samples. Although the

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reference is silent to the teaching of “code”, it was well known and commonly practiced that Microsoft Excel (see page 211) is a software product containing code used to generate graphs. Through the use of this code, Zhao et al generated the graphs depicted in Figure 3 to compare the expression level of two different samples. Moreover, the computer used was a Macintosh computer(see page 211) as depicted in Figure 1. Although the reference is silent to the teaching of processor, memory and display, the personal computer inherently contains a display, microprocessor and memory in the form of RAM, ROM and hard disk.

Zhao et al do not specifically teach an input from user and returning information of the selected expressed sequence.

Seilhamer et al teach preparing a relational database for a computer system that contains cDNA sequencing data and corresponding match logs indicating a correlation between presently identified cDNA sequences and previously known sequences. These databases may be organized in a table. They teach that a researcher to search the relational database using keywords or a query and to specify a search on the table to seek out specific information (See all of page 17). They teach that these databases and queries assist the scientist in performing many and various data analysis tasks.

One of ordinary skill in the art would have been motivated to apply Seilhamer et al’s use of database in a computer system to Zhao et al’s computer system and method of analyzing expression in samples in order to quickly allow user to gain information on the expressed sequences. Zhao et al states that the sequences for the cDNA probes were determined prior to

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preparing the filter. It would have been prima facie obvious to one of ordinary skill in the art to incorporate Zhao predetermined sequence information into a Seilhamer et al's database for the computer in order to allow the practitioner to input a query and easily access to information to assist in various data analysis tasks.

Moreover, one of ordinary skill in the art would have been motivated to implement the Microsoft Excel program in code format to display the expression level in order to analyze various data inputs from various samples on different platforms. A program code provides versatility in allowing dynamic input to be analyzed. It would have been advantageous to implement analysis and display on code so that a large number of different samples would be analyzed especially over time. Moreover, the implementation on code would allow the analysis to be performed across different platforms and even different machines. It would have been prima facie obvious to implement the display of the expression levels through a computer code comprising code in order to analyze and display a constantly changing and new input across different platforms and machines.

Moreover, one of ordinary skill in the art would have been motivated to to display the expression level on a computer system containing display, processor and memory in order to analyze various data inputs from various samples. A computer system provides excellent data storage and data manipulation capabilities. It would have been advantageous to implement analysis and display on a computer system so that a large number of different samples would be

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analyzed. It would have been prima facie obvious to implement the display of the expression levels on a computer system in order to analyze large amounts of data efficiently.

5. Claim 19 & 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhao et al (Gene Vol. 156 pp. 207-213 1995) in view of Seilhamer et al (WO96/23078 1 August 1996).

Claim 19 is drawn to claim 1 with the further limitation of displaying third axis wherein the mark is position relative to expression level of a third sample.

Claim 43 is drawn to claim 25 a computer product with the further limitation of having code displaying third axis wherein the mark is position relative to expression level of a third sample

The teachings and suggestions of Zhao et al and Seilhamer et al are described previously, briefly they teach bioimaging analyzer system to compare the expression profiles of thousands of genes cDNAs) simultaneously. They teach the a high density cDNA filter analysis in which expression profiles of 2505 cloned human brain cDNAs (genes) were monitored (see whole document esp. Abstract). Zhao et al also teaches that the cDNA probes were sequenced and compared with those in GenBank DNA nucleotide sequence Database by BLASTN program prior to preparing the filter. A quantitative analysis of the filter is performed using Fuji Bioimaging Analyzer BAS2000 System and automated quantification program AutoQuant. The final part is sequence analysis in which each clone is characterized by homology search in the GENBANK nucleotide Sequence Database (see page 208 & Figure 1). They applied the system for the

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comparative analysis of expression profile of the human cDNAs in brain. The expression profiles were illustrated on graphs by comparing the their scores from two tissues with Microsoft Excel (Microsoft) on a Macintosh personal computer(see page 210-211 and fig. 3). A mark for each gene is positioned relative to the expression levels in the two different samples. Although the reference is silent to the teaching of “code”, it was well known and commonly practiced that Microsoft Excel (see page 211) is a software product containing code used to generate graphs. Through the use of this code, Zhao et al generated the graphs depicted in Figure 3 to compare the expression level of two different samples. Moreover, the computer used was a Macintosh computer(see page 211) as depicted in Figure 1. Although the reference is silent to the teaching of processor, memory and display, it was well known and commonly practiced in the art that personal computer contains a display, microprocessor and memory in the form of RAM, ROM and hard disk.

Seilhamer et al teach preparing a relational database for a computer system that contains cDNA sequencing data and corresponding match logs indicating a correlation between presently identified cDNA sequences and previously known sequences. These databases may be organized in a table. They teach that a researcher to search the relational database using keywords or a query and to specify a search on the table to seek out specific information (See all of page 17). They teach that these databases and queries assist the scientist in performing many and various data analysis tasks.

Zhao et al do not teach a third axis.

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One of ordinary skill in the art would have been motivated to apply a third axis to Zhao et al display format in order to further compare the expression level in a third sample. It would have been advantageous to use a 3D format to compare three samples at the same time so that comparisons would be visually easier to interpret and would be performed simultaneously. It would have been prima facie obvious to apply a third axis to Zhao et al's display format in order to analyze more information at the same time.

6. Claims 6-10,12-18 & 30-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al (WO97/27317 21 July 1997) in view of Zhao et al (Gene Vol. 156 pp. 207-213 1995) in further view of Seilhamer et al (WO96/23078 1 August 1996).

Claims 6-10 & 12-18 are drawn to claim 1 in which the expression level of expressed sequence is monitored and plurality of hybridization intensities from pairs of matched and unmatched probes are inputted.

Claims 30-34 are drawn to claim 29 with the added limitation that the code further allows input of plurality of hybridization intensities from pairs of matched and unmatched probes.

Lockhart et al teach a method of detecting nucleic acid abundances or concentrations (e.g. expression levels) between two or more samples (see whole document esp. abstract). They teach the simultaneous monitoring of the expression of a multiplicity of genes using perfect match probe and mismatch probes (see page 5,12,47 & esp. 49-50). They teach that expression monitoring would be useful for both drug safety and toxicology screenings (see page 230) and monitoring

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various genes in response to defined stimuli such as drugs (see page 22). They teach that monitoring of gene expression may be performed using a computer system running a software program that includes computer code incorporating analysis of hybridization intensities of the screens(see page 90 & Figure 6-8). They teach a method of comparing expression level using the hybridization intensities between the perfect match and mismatch probes (see page 93-101 & Figure 9-10B). They compare the hybridization intensity difference and ratio of the perfect match and mismatch probes with a threshold. The values NPOS, NNEG and LR are calculated for each pair of probes. The analysis is repeated to calculate the average of the differences. They teach that oligonucleotide pairs that show the greatest differential hybridization between two samples can be identified by sorting the observed hybridization ratio and difference values. Based on identified oligonucleotide pair sequences, a gene can be searched for in sequence databases such as GENBANK (see page 128-9). They also display the results in a graph showing differential expression between samples (see Figures 16-17).

Lockhart et al do not teach presenting expression level information by displaying on a first axis representing the expression level in a first sample, displaying on second axis representing the expression level in the second axis and displaying a mark relative to the two axes. Lockhart does not teach an input from user and returning information of the selected expressed sequence.

Zhao et al teach bioimaging analyzer system to compare the expression profiles of thousands of genes cDNAs) simultaneously . They teach the a high density cDNA filter analysis in which expression profiles of 2505 cloned human brain cDNAs (genes) were monitored (see whole

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document esp. Abstract). Zhao et al also teaches that the cDNA probes were sequenced and compared with those in GenBank DNA nucleotide sequence Database by BLASTN program prior to preparing the filter. A quantitative analysis of the filter is performed using Fuji Bioimaging Analyzer BAS2000 System and automated quantification program AutoQuant. The final part is sequence analysis in which each clone is characterized by homology search in the GENBANK nucleotide Sequence Database (see page 208 & Figure 1). They applied the system for the comparative analysis of expression profile of the human cDNAs in brain. The expression profiles were illustrated on graphs by comparing the their scores from two tissues with Microsoft Excel (Microsoft) on a Macintosh personal computer(see page 210-211 and fig. 3). Although the reference is silent to the teaching of processor, memory and display, the personal computer inherently contains a display, microprocessor and memory in the form of RAM, ROM and hard disk.

Seilhamer et al teach preparing a relational database for a computer system that contains cDNA sequencing data and corresponding match logs indicating a correlation between presently identified cDNA sequences and previously known sequences. These databases may be organized in a table. They teach that a researcher to search the relational database using keywords or a query and to specify a search on the table to seek out specific information (See all of page 17). They teach that these databases and queries assist the scientist in performing many and various data analysis tasks.

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One of ordinary skill in the art would have been motivated to display the comparative expression levels of genes as in Zhao et al's to Lockhart et al's analysis technique in order to compare the gene expression between two different samples. Zhao et al's display format allows easy visualization of the many different expressions of genes between two samples. It would have been prima facie obvious to construct a graph with an axis representing the gene expression in one sample and another axis representing the gene expression in a second sample in order to compare the differential gene expression between the different samples.

Moreover, one of ordinary skill in the art would have been motivated to apply Seilhamer et al's use of database in a computer system to Zhao et al's computer system and method of analyzing expression in samples in order to quickly allow user to gain information on the expressed sequences. Zhao et al states that the sequences for the cDNA probes were determined prior to preparing the filter. It would have been prima facie obvious to one of ordinary skill in the art to incorporate Zhao predetermined sequence information into a database for the computer in order to allow the practitioner to easily access to information to assist in various data analysis tasks.

7. Claims 22, 24 & 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhao et al in view of Seilhamer et al (WO96/23078 1 August 1996) in further view Beattie (US5,843,767 December 1, 1998).

Claims 22 & 24 are drawn to claim 20 with the added limitation the polymer is a protein.

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Claim 46 is drawn to claim 44, a computer product with the added limitation the polymer is a protein.

The teachings and suggestions of Zhao et al and Seilhamer et al are described above.

Zhao et al do not teach the use of protein polymers.

Beattie et al teach the use of protein probes such as antibodies in hybridization array (see whole document).

One of ordinary skill in the art would have been motivated to apply Beattie et al's teaching of using protein probes to Zhao et al's expression display in order to compare the expression level of actual translated protein between two samples. Beattie states that the use of antibodies or ligand receptor binding would be applicable to the study of identifying biomolecules. It was well known and commonly practiced to use these ligand -receptor binding techniques in order to actually identify the stage of gene expression i.e. the translated protein. It would have been prima facie obvious to use Beattie's protein probes and display the results between two samples using Zhao et al's expression method in order to compare the protein levels which represent the final stage of gene expression

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SUMMARY

8. No claims allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

CONCLUSION

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Siew whose telephone number is (703) 305-3886 and whose e-mail address is Jeffrey.Siew@uspto.gov. The examiner can best be reached on Monday through

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Thursday from 6:30 a.m. to 4 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brad Sisson, can be reached on (703) 308-3978.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist for Technology Center 1600 whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Center numbers for Group 1600 are Voice (703) 308-3290 and Fax (703) 305-3014 or (703) 308-4242.



Jeffrey Siew

October 5, 1999

KENNETH R. HORLICK
PRIMARY EXAMINER
GROUP 1600 10/7/99

